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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,058	03/17/2004	Anuj Chauhan	T2315-908542US02	1707

181 7590 09/25/2009

MILES & STOCKBRIDGE PC
1751 PINNACLE DRIVE
SUITE 500
MCLEAN, VA 22102-3833

EXAMINER	
BERRIOS, JENNIFER A	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
09/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocketing@milesstockbridge.com
sstiles@milesstockbridge.com

Office Action Summary	Application No.	Applicant(s)	
	10/802,058	CHAUHAN ET AL.	
	Examiner	Art Unit	
	Jennifer A. Berrios	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2008 and 15 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/30/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants request for continued examination filed on 10/16/2008 has been acknowledged.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/16/2008 has been entered.

This office action is in response to the reply filed 8/15/2008 and 11/5/2008, wherein claims 1-8 have been amended and claim 20-21 are newly added.

Currently claims 1-21 are pending examination.

Information Disclosure Statement

Applicant's Informational Disclosure Statement, filed on 5/30/2008 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Oath/Declaration

Acknowledgement is made of the declaration filed 8/15/2008.

Withdrawn Rejection

All rejection present in the office action mailed 4/16/2008 have been withdrawn due to claim amendment, except the 112 2nd Paragraph rejection of claims 1-21, as being indefinite.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 includes the limitation "wherein said diffusion provides extended or time-release delivery of said ophthalmic drug". Said limitation is indefinite because diffusion doesn't provide release characteristics; the materials utilized do. Claims 2-21 all depend ultimately from claim 1.

New Rejections

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-5, 7-15 and 20-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Resnick (US 2002/0141760), Ding (PSTT, Vol. 1, No. 8, Nov 1998), Vandamme (Progress in Retinal and Eye Research 21 (2002)15-34), Nagarsenker et al (Int. Journal of Pharmaceutics 190 (1999) 63-71) and Paul et al (Current Science, Vol. 80, No. 8, 25 April 2001).

Regarding claims 1, 3-4, 9 and 12: Resnick teaches a contact lens containing nanospheres that are incorporated directly therein (paragraphs 0003 and 0006). Resnick further teaches methods of incorporating drugs and therapeutic agents into the contact lens for the purpose of drug delivery to the eye (paragraph 0019 and claim 2) as well as a kit (title; fig. 3). Resnick refers to US patents 5,891,932 and 4,865,439 in paragraph 0006 for their teaching of typical contact lenses that Resnick uses as starting materials. Said patents teach soft contact lenses and incorporation of 2-hydroxyethylmethacrylate as well as storing the lenses in saline solution.

Resnick is silent to the phrase "optically transparent", however the definition of said term in applicant's specification states, "a degree of transparency equivalent to that of p-HEMA or other material employed as a contact lens". The materials taught in Resnick read on said definition.

Ding is cited to demonstrate that it's well known in the art that nanoparticles can be utilized, which provide sustained drug release and prolonged therapeutic activity for the delivery of either hydrophobic or hydrophilic ophthalmic drugs (Pg 332-333). Furthermore controlled particle size and control of the rate of the drug release must be further examined.

Regarding claim 2: Resnick teaches microsphere with an approximate diameter of .25 micrometers (approx 250nm). It would have been obvious to one of skill in the art to optimize the size of the nanoparticles dependent on the desired purpose and desired results, as taught by Ding, absent any evidence of criticality. Furthermore it would have

been obvious to one of skill in the art to distribute the nanoparticles in such as manner that optical transparency is maintained.

Regarding claims 3 and 21: Claims 3 and 21 claims that the amount of nanoparticles is from about 1-5% and from 5-20%. It would have been obvious to one of skill in the art through routine experimentation to determine the amount of nanoparticles necessary to achieve desired results, while maintaining the optical transparency of the contact lens.

Regarding claims 10-11 and 14-15: Resnick is silent to the particulars of the kit claimed in the instant claims.

It is well within the knowledge of one of ordinary skill in the art to include a kit or article of manufacture because they provide a convenient mechanism to disperse products to consumers. Additionally, labels containing indications, directions, warnings, etc. are mandated. A practitioner would reasonably expect a kit comprising the drug delivery system of Resnick to provide a convenient mechanism to disperse the product to consumers as well as inform the consumer of indications, directions, and so on. Therefore, in Resnick it would have been obvious to one of ordinary skill in the art to package and label delivery system in a kit or article of manufacture.

It is also well within the knowledge of one of ordinary skill in the art to include a drug-saturated solution in the kit so the drug does not diffuse out of the contact lens and become diluted. A practitioner would reasonably expect the contact lens to have a therapeutically effective amount or concentration of drug. Therefore, in Resnick it would

have also been obvious to one of ordinary skill in the art to include a drug-saturated solution in a kit or article of manufacture.

Resnick fails to teach the ophthalmic drug nanoparticles to be encapsulated with an encapsulation material selected dependent on the drug characteristic (hydrophobic or hydrophilic), such as liposome's or micro emulsions as recited by instant claims 1, 5 and 8 and the ophthalmic drug being pilocarpine, as recited by instant claim 21.

Vandamme teaches micro emulsions as ocular drug delivery systems, which are thermodynamically stable and inherently provide the capacity to make soluble lipophilic drugs (Pg. 16). The main advantage of the micro-emulsion is the increase in the solubilization of drugs. Table 4 demonstrates a microemulsion containing the drug pilocarpine. Paul further teaches that micro-emulsions allow sustained release or controlled drug release for ocular administration (Pg 995).

Nagarsenker teaches the preparation and evaluation of liposomal formulations for ocular delivery, which can serve as a slow release depot. Ophthalmic drugs were entrapped in liposomes. Liposome's have the ability to entrap hydrophilic compounds in the aqueous compartment and to incorporate hydrophobic molecules in the lipid bilayers (Pg 64).

Both Vandamme and Nagarensker teach encapsulation materials, liposomes and micro emulsions that can be used with hydrophilic or lipophilic (which are hydrophobic).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to combine to teaching of Resnick/Vandamme and Nagarensker to arrive at the instant invention. One of skill in the art would have been motivated to

select one of the encapsulations materials, micro encapsulation or liposome's as taught by Vandamme and Nagarensker depending on the drug utilized in the nanoparticles, hydrophobic or hydrophilic, as Vandamme teaches that micro emulsions make lipophilic drugs more soluble and liposomes are efficient for slow release depot of drugs. Finally one of skill in the art would expect reasonable success because Resnick/Vandamme/Nagarensker all teach controlled release ocular drug delivery.

Response to Arguments

In the replies filed 11/5/2008 and 8/15/2008 and the declaration filed 8/15/2008 applicant argues that Resnick does not have an enabling disclosure for the instant invention. Applicant further provides a list of things, such as particle size, drug concentration, etc that Resnick is not enables for. This is not found persuasive because applicant has failed to demonstrate and has not provided evidence that the reference must teach these things. Applicant has not demonstrated that one of skill in the art would not come with that knowledge. As demonstrated, in the above rejection Ding teaches that use of nanoparticles for controlled drug delivery release and teaches that factors such as particle size, needs to be further investigates, therefore one of skill in the art would understand that in order to achieve an ideal drug delivery rate, it's necessary to determine the ideal particle size, and certain amounts of routine experimentation would be required. In the filed declaration applicant argues that factors such as correct size and type of the nanoparticles is critical, but has not provided any

factual evidence demonstrating this, nor demonstrating which particular size and type is critical.

In the 11/5/2008 reply, applicant further argues that Resnick does not teach ophthalmic drugs, but disclosed encapsulating reflective or radiant energy adsorptive materials, all which are harmful to the to the eye if allowed to diffuse out of the nanoparticles and therefore would not be regarded by a person of skill in the art at as an ophthalmic drug. This is not found persuasive because Resnick clearly teaches "drug delivery" at paragraph [0019] and claims 2 and 12, as such it would have been obvious that the nanoparticles could be modified to include ophthalmic/ocular drugs, safe for the eye, for drug release.

6. Claims 6 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Resnick (US 2002/0141760), Ding (PSTT, Vol. 1, No. 8, Nov 1998), Vandamme (Progress in Retinal and Eye Research 21 (2002)15-34), Nagarsenker et al (Int. Journal of Pharmaceutics 190 (1999) 63-71) and Paul et al (Current Science, Vol. 80, No. 8, 25 April 2001) as applied to claims 1-5, 7-15 and 20-21 above, and further in view of Darouger et al (US 6,264,971).

Resnick/Vandamme/Nagarsenker teach the elements of claim 1, but are silent to the particular ophthalmic drugs recited in claims 6 and 17-19.

Darougar teaches an ocular insert that release an ophthalmic drug in a controlled, sustained fashion (abstract). Said ophthalmic drugs include antibiotics such

as gentamycin, anti-microbial drugs, anti-inflammatories such as prednisolone acetate, non-steroidal agents such as diclofenac (i.e., Voltaren), pilocarpine and timolol (col. 5, line 41 – col. 6, line 16). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include said particular ophthalmic drugs in nanoparticles in the contact of Resnick with a reasonable expectation of success because the prior art suggests that a) said drugs are well-known for the purpose of treating the eye an can be used in controlled release devices.

Response to Arguments

In the reply filed on 8/15/2008, applicant argues that the geometry of the device plays a very important role on the drug delivery rates to the cornea and that the teaching of Darougar a substantially different from the instant claims. This is not found persuasive because applicant has not provided factual evidence demonstrating that the criticality of the geometry of the drug delivery device and furthermore applicant is arguing drug delivery rate, a limitations not found in the instant claims.

7. Claims 6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Resnick (US 2002/0141760), Ding (PSTT, Vol. 1, No. 8, Nov 1998), Vandamme (Progress in Retinal and Eye Research 21 (2002)15-34), Nagarsenker et al (Int. Journal of Pharmaceutics 190 (1999) 63-71) and Paul et al (Current Science, Vol. 80, No. 8, 25 April 2001) as applied to claims 1-5, 7-15 and 20-21 above, and further in view of Raut (US 2003/0216431).

Resnick/Vandamme/Nagarsenker teach the elements of claim 1, but are silent to the particular ophthalmic drugs recited in claims 6 and 16.

Raut teaches ophthalmic pharmaceutical compositions for topical administration to the eye (abstract). In a particular embodiment, Raut includes pyrimethamine (paragraph [0117]). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include pyrimethamine in nanoparticles in the contact of Resnick with a reasonable expectation of success because the prior art suggests that pyrimethamine is well-known for the purpose of treating the eye and Resnick disclosed drug delivery for ocular use.

Response to Arguments

In the reply filed 8/15/2008 applicant argues that it is essential that the nanoparticles have a very high partition coefficient effect for the drug and with out undue experimentation it would not be obvious to one of skill in the art to incorporate the pyrimethamine taught by Raut into the lens taught by Resnick. This is not found persuasive because applicant is arguing limitations not found in the instant claims (partition coefficient).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JB

/SUE LIU/
Primary Examiner, Art Unit 1639